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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,864	09/18/2003	Zhuyin Julie Li	USA V2002/0121 US NP	8381

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ROSS J. OEHLER
SANOFI-AVENTIS U.S. LLC
1041 ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
KIM, TAEYOON	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,864	LI ET AL.	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on Dec. 13, 2006 has been received and entered into the case.

Claims 1-25 are pending and have been considered on the merits. All arguments have been fully considered.

Response to Arguments

Applicant argues that the references used in the rejections under 35 U.S.C.§103(a) in the previous office action mailed on Sept. 8, 2006 failed to teach or suggest all limitations and there is no suggestion or motivation to modify or combine reference teachings to produce claimed invention. This is because the references do not teach shorter duration time of the assay with simpler steps as the claimed invention.

This argument is not persuasive because the current invention dose not claim limitations of shortened duration of assay time and/or simpler steps. Although the specification indicates that the current invention would have advantages over other PARP assays because it has overcome the shortcomings of the prior art assays, however, such limitations were not claimed in the current application. Claims 1-25 do not disclose that the current invention does not require multiple washing steps and/or shorter assay time. Rather, the incubation time of the assay is claimed to be at least 2 hours in the current invention, which could be overnight (see claim 1 and its dependents).

Further, applicant argues that total hours of assay disclosed in the references (i.e. Decker et al. and Trevigen) is disclosed as "overnight or at least 7 hours or more"

which includes preparation time of enzyme coating and reagent. It is noted that in claim 1 and its dependents, applicant recites the phrases "comprising," which is open-claim language. The transitional phrases "comprising", "consisting essentially of" and "consisting of" define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, *e.g.*, *Invitrogen Corp. v. Biocrest Mfg.*, L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003). The transition "comprising" in a method claim indicates that the claim is open-ended and allows for additional step. See M.P.E.P. §2111.03. Because the use of open-ended language in the claims, the current invention could have steps of preparation of reagents (e.g. immobilization of PARP enzyme on the plates) as well as multiple washing steps. Therefore, it is only fair to compare actual incubation and measurement steps between the prior art references and the current invention. The incubation duration disclosed in Decker et al. as well as Trevigen is both 1 hr, which is well within the range of incubation step claimed in the current invention (i.e. from about 10 minutes to at least about 2 hours in claim 3).

Still further, the combination of references (i.e. Decker et al. in view of Corominas et al. and Armstrong et al.) would be beneficial as discussed in the previous office action that a person of ordinary skill in the art would recognize that the use of labeled NAD+ is more efficient than the use of a non-labeled NAD+ in PARP assay because it can be directly detected without employing another step using an anti-poly(ADP-ribose)

and a secondary antibody against the anti-poly(ADP-ribose). This would provide not only a motivation for a person of ordinary skill in the art to use a labeled NAD+ in the method of Decker et al., but also eliminates additional washing steps required in indirect detection system.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made based on the prior art references cited in the previous office action.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Decker et al. in view of Corominas et al. and Armstrong et al.

Decker discloses a PARP inhibition assay which differs from that recited in the claims in that Decker does not use fluorescently labeled NAD in the quantification of enzyme activity. See, e.g., Fig 1, on page 1170. However, Corominas et al. clearly discloses that labeled NAD can be used in the quantification of PARP activity. See, e.g., page 16270, left column. Moreover, Armstrong discloses the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme, an assay which detects similar activity to that of both Decker and Corominas. See, e.g., page 28. Thus, the artisan of ordinary skill would have considered it obvious to have used fluorescently labeled NAD in the quantification of enzyme activity in Decker's assay, motivation for such practice being derived from Corominas' disclosure of the suitability of labeled NAD as detection

moiety in PARP assays, and from Armstrong's disclosure of the suitability of fluorescently labeled NAD as a detection moiety in a similar assay of ADP-ribosylating enzyme. Moreover, the selection of known fluorescent moieties, and the determination of suitable linking moieties therefor as recited in the claims under examination, would have been considered obvious in view of the cited references' disclosures of the suitability of using fluorescently labels to detect NAD. A holding of obviousness is therefore required.

Claims 1-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Trevigen (Universal Colorimetric PARP Assay kit with histones and coating buffer, 2000; http://www.trevigen.com/Protocols/4671_4672-096-K.pdf) in view of Armstrong et al. (supra), Sundberg (Current Opinion in Biotechnology, 2000, 11:47–53) and Human Molecular Genetics (Fluorescence labeling and detection system, 1999; http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hmg.table.479)

It is noted that although the published date of the Trevigen article is not clearly established, this assay kit utilizing a biotinylated NAD+ for PARP assay has been disclosed by an article entitled to New Technology (Nature Medicine, 2000, 6:715;). Therefore, the Examiner considers the reference as a prior art to the filing date of the current application.

The Trevigen reference teaches a method of determining inhibitors on the activity of PARP comprising steps of incubation of PARP enzyme, an inhibitor, a substrate (biotinylated NAD+, DNA, histone), detection of enzymatic activity, and comparison of the measurement (see pages 1-4).

The Trevigen article does not teach the use of fluorescently labeled NAD+ in an assay.

Armstrong et al. teach the use of fluorescently labeled NAD in an assay of ADP-ribosylating enzyme.

Sundberg teaches fluorescence-based biochemical assays.

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to substitute biotinylated NAD+ of Trevigen with fluorescently labeled NAD+ of Armstrong et al. in the method of Trevigen Instruction.

The skilled artisan would have been motivated to make such a modification because Sundberg teach that fluorescence-based detection methods are inherently sensitive due to the short duty cycle of most fluorophores (the fluorescence lifetime of fluorescein is ~4 ns) and consequently high emitted photon fluxes that can be achieved even with modest excitation light sources. This property, combined with the variety of different fluorescence modes that can be exploited to advantage in homogeneous assay formats, makes fluorescence detection highly amenable to many high-throughput screening applications (see page 47, right column).

The person of ordinary skill in the art would have had a reasonable expectation of success in substituting biotinylated NAD+ with fluorescence-labeld NAD+ because fluorescence labeling has been well known and practiced in the art.

M.P.E.P. §2144,06 states "In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components

at issue are functional or mechanical equivalents. In re Ruff, 256 F.2d 590, 118 USPQ 340 (CCPA 1958) (The mere fact that components are claimed as members of a Markush group cannot be relied upon to establish the equivalency of these components. However, an applicant's expressed recognition of an art-recognized or obvious equivalent may be used to refute an argument that such equivalency does not exist.); In re Scott, 323 F.2d 1016, 139 USPQ 297 (CCPA 1963)."

Therefore, the substitution of biotinylation from Trevigen Instruction of the fluorescently labeled NAD+ of Armstrong et al. in an assay of ADP-ribosylating enzyme would have been obvious because Sundberg discloses colorimetric, fluorescent or luminescent read-out as an alternative method for a detection/quantification system (p. 49, right column). Therefore, these may be considered to be art-accepted equivalents.

In addition, various different fluorescence labels such as Texas red, rhodamine, or CyDye are well known equivalents for fluorescent labeling of chemicals as supported by Human Molecular Genetics (supra).

One of skill in the art would have been motivated at the time of invention to make this substitution in order to quantify the PARP activity as suggested by Trevigen with a reasonable expectation of success. The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Taeyoon Kim
Patent Examiner
Art Unit 1651

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651